

REPLACEMENT SHEET



Figure 1

MAMSSGGSGGGVPEQEDSVLFRRGTGQSDSDIWDDTALIKAYDKAVASFKHALKNG
DICETSGKPKTTTPKRKPAKKNKSQKKNTAASLQQWKVGDKCSAIWSEDGCIYPATIA
SIDFKRETCVVVYTYGYNREEQNLSDLLSPICEVANNIEQNAQENENESQVSTDESE
NSRSPGNKSDNIKPKSAPWNSFLPPPPMPGPRLGPGKPGGLKFNGPPPPPPPPPHL
LSCWLPPFPSPGPPIIPPPPPICPDSLDDADALGSMLISWYMSGYHTGYMGMFRQNQK
EGRCSHSLN

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Figure 2A

CGGGGCCCCACGCTGCGCACCCGCGGGTTTGCTATGGCGATGAGCAGCGGCGGCAGT
GGTGGCGGCGTCCCGGAGCAGGAGGATTCCGTGCTGTTCCGGCGCGGCACAGGCCAG
AGCGATGATTCTGACATTTGGGATGATACAGCACTGATAAAAGCATATGATAAAGCT
GTGGCTTCATTTAAGCATGCTCTAAAGAATGGTGACATTTGTGAAACTTCGGGTAAA
CCAAAACCACACCTAAAAGAAAACCTGCTAAGAAGAATAAAAGCCAAAAGAAGAAT
ACTGCAGCTTCCTTACAACAGTGGAAGTTGGGGACAAATGTTCTGCCATTTGGTCA
GAAGACGGTTGCATTTACCCAGCTACCATTGCTTCAATTGATTTTAAGAGAGAAACC
TGTGTTGTGGTTTACACTGGATATGGAAATAGAGAGGAGCAAAATCTGTCCGATCTA
CTTTCCCCAATCTGTGAAGTAGCTAATAATATAGAACAGAATGCTCAAGAGAATGAA
AATGAAAGCCAAGTTTCAACAGATGAAAGTGAGAACTCCAGGTCTCCTGGAAATAAA
TCAGATAACATCAAGCCCAAATCTGCTCCATGGAACCCCTTTCTCCCTCCACCACCC
CCCATGCCAGGGCCAAGACTGGGACCAGGAAAGCCAGGTCTAAAATTCAATGGCCCA
CCACCGCCACCGCCACCACCACCACCCCACTTACTATCATGCTGGCTGCCTCCATTT
CCTTCTGGACCACCAATAATTCCCCCACCACCTCCCATATGTCCAGATTCTCTTGAT
GATGCTGATGCTTTGGGAAGTATGTTAATTTTCATGGTACATGAGTGGCTATCATACT
GGCTATTATATGGGTTTTAGACAAAATCAAAAAGAAGGAAGGTGCTCACATTCCTTA
AATTAAGGAGAAATGCTGGCATAGAGCAGCACTAAATGACACCACTAAAGAAACGAT
CAGACAGATCTGGAATGTGAAGCGTTATAGAAGATAACTGGCCTCATTTCCTCAAAA
TATCAAGTGTTGGGAAAGAAAAAAGGAAGTGGAATGGGTAACTCTTCTTGATTAAAA
GTTATGTAATAACCAAATGCAATGTGAAATATTTTACTGGACTCTTTTGAAAAACCA
TCTGTAAAAGACTGAGGTGGGGGTGGGAGGCCAGCACGGTGGTGAGGCAGTTGAGAA
AATTTGAATGTGGATTAGATTTTGAATGATATTGGATAATTATTGGTAATTTTATGG
CCTGTGAGAAGGGTGTTGTAGTTTATAAAAGACTGTCTTAATTTGCATACTTAAGCA
TTTAGGAATGAAGTGTTAGAGTGTCTTAAATGTTTCAAATGGTTTAACAAAATGTA
TGTGAGGCGTATGTGGCAAAATGTTACAGAATCTAACTGGTGGACATGGCTGTTTCAT
TGTA CTGTTTTTTTCTATCTTCTATATGTTTAAAAGTATATAATAAAAATATTTAAT
TTTTTTTTAA
AA



REPLACEMENT SHEET

Figure 2B

AATTTTAAATTTTTGTAGAGACAGGGTCTCATTATGTTGCCCAGGGTGGTGTCAA
GCTCCAGGTCTCAAGTGATCCCCCTACCTCCGCCTCCCAAAGTTGTGGGATTGTAGG
CATGAGCCACTGCAAGAAAACCTTAACTGCAGCCTAATAATTGTTTTCTTTGGGATA
ACTTTTAAAGTACATTAAAAGACTATCAACTTAATTTCTGATCATATTTTGTGGAAT
AAAATAAGTAAAATGTCTTGTGAACAAAATGCTTTTTAACATCCATATAAAGCTATC
TATATATAGCTATCTATATCTATATAGCTATTTTTTTTTAACTTCCTTTTATTTTCCT
TACAG*GGTTTTAGACAAAATCAAAAAGAAGGAAGGTGCTCACATTCCTTAAATTAA
GGA*GTAAGTCTGCCAGCATTATGAAAGTGAATCTTACTTTTGTAACCTTTATGGT
TTGTGGAAAACAAATGTTTTTGAACAGTTAAAAAGTTCAGATGTTAGAAAGTTGAAA
GGTTAATGTAAAACAATCAATATTAAAGAATTTTGATGCCAAAACCTATTAGATAAAA
GGTTAATCTACATCCCTACTAGAATTCTCATACTTAACTGGTTGGTTGTGTGGAAGA
AACATACTTTCACAATAAAGAGCTTTAGGATATGATGCCATTTTATATCACTAGTAG
GCAGACCAGCAGACTTTTTTTTTATTGTGATATGGGATAACCTAGGCATACTGCACTG
TACACTCTGACATATGAAGTGCTCTAGTCAAGTTTAACTGGTGTCCACAGAGGACAT
GGTTTAACTGGAATTCGTCAAGCCTCTGGTTCTAATTTCTCATTTGCAG*GAAATGC
TGGCATAGAGCAGCACTAAATGACACCCTAAAGAAACGATCAGACAGATCTGGAAT
GTGAAGCGTTATAGAAGATAACTGGCCTCATTCTTCAAATATCAAGTGTTGGGAA
AGAAAAAAGGAAGTGGAATGGGTAACCTCTTCTTGATTAAAAGTTATGTAATAACCAA
ATGCAATGTGAAATATTTTACTGGACTCTTTTGAAAAACCATCTGTAAAAGACTGAG
GTGGGGGTGGGAGGCCAGCACGGTGGTGAGGCAGTTGAGAAAATTTGAATGTGGATT
AGATTTTGAATGATATTGGATAATTATTGGTAATTTTATGGCCTGTGAGAAGGGTGT
TGTAGTTTATAAAAGACTGTCTTAATTTGCATACTTAAGCATTTAGGAATGAAGTGT
TAGAGTGTCTTAAAATGTTTCAAATGGTTTAAACAAAATGTATGTGAGGCGTATGTGG
CAAAATGTTACAGAATCTAACTGGTGGACATGGCTGTTTCATTGTACTGTTTTTTCT
ATCTTCTATATGTTTAAAAGTATATAATAAAAATATTTAATTT



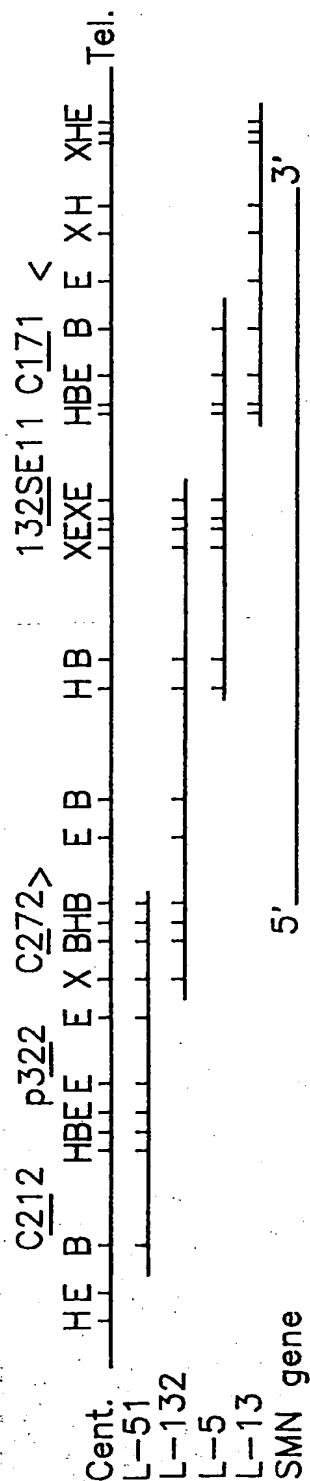
REPLACEMENT SHEET

Figure 3B

AATTTTAAATTTTTGTAGAGACAGGGTCTCATTATGTTGCCCAGGGTGGTGTCAA
GCTCCAGGTCTCAAGTGATCCCCCTACCTCCGCCTCCCAAAGTTGTGGGATTGTAGG
CATGAGCCACTGCAAGAAAACCTTAACTGCAGCCTAATAATTGTTTTCTTTGGGATA
ACTTTTAAAGTACATTAAAAGACTATCAACTTAATTTCTGATCATATTTTGTGAAT
AAAATAAGTAAAATGTCTTGTGAACAAAATGCTTTTTAACATCCATATAAAGCTATC
TATATATAGCTATCTATGTCTATATAGCTATTTTTTTTTAACTTCCTTTTATTTTCCT
TACAG*GGTTTCAGACAAAATCAAAAAGAAGGAAGGTGCTCACATTCCTTAAATTAA
GGA*GTAAGTCTGCCAGCATTATGAAAGTGAATCTTACTTTTGTAACCTTTATGGT
TTGTGGAAAACAAATGTTTTTGAACAGTTAAAAAGTTCAGATGTTAAAAAGTTGAAA
GGTTAATGTAAAACAATCAATATTAAAGAATTTTGATGCCAAAACCTATTAGATAAAA
GGTTAATCTACATCCCTACTAGAATTCTCATACTTAACTGGTTGGTTATGTGGAAGA
AACATACTTTCACAATAAAGAGCTTTAGGATATGATGCCATTTTATATCACTAGTAG
GCAGACCAGCAGACTTTTTTTTTATTGTGATATGGGATAACCTAGGCATACTGCACTG
TACACTCTGACATATGAAGTGCTCTAGTCAAGTTTAACTGGTGTCCACAGAGGACAT
GGTTTAACTGGAATTCGTCAAGCCTCTGGTTCTAATTTCTCATTTCAG*GAAATGC
TGGCATAGAGCAGCACTAAATGACACCACTAAAGAAACGATCAGACAGATCTGGAAT
GTGAAGCGTTATAGAAGATAACTGGCCTCATTTCCTTCAAAATATCAAGTGTTGGGAA
AGAAAAAAGGAAGTGGAATGGGTAACCTCTTCTTGATTAAAAGTTATGTAATAACCAA
ATGCAATGTGAAATATTTTACTGGACTCTTTTGAAAAACCATCTGTAAAAGACTGGG
GTGGGGGTGGGAGGCCAGCACGGTGGTGAGGCAGTTGAGAAAATTTGAATGTGGATT
AGATTTTGAATGATATTGGATAATTATTGGTAATTTTATGGCCTGTGAGAAGGGTGT
TGTAAGTTTATAAAAGACTGTCTTAATTTGCATACTTAAGCATTTAGGAATGAAGTGT
TAGAGTGTCTTAAAATGTTTCAAATGGTTTAAACAAAATGTATGTGAGGCGTATGTGG
CAAAATGTTACAGAATCTAACTGGTGGACATGGCTGTTTCAATTGTACTGTTTTTTCT
ATCTTCTATATGTTTAAAAGTATATAATAAAAATATTTAATTT

TCCACCCGCCTTGGCCTCCCAAAGCNCTGGGATTACAGGCGTGACTGCCGCACCCAG
CTGTAAACTGGNTTNNTAATGGTAGATTTTNAGGTATTAACAATAGATAAAAAGATA
CTTTTNGGCATACTGTGTATTGGGATGGGGTTAGAACAGGTGTNCTACCCAAGACAT
TACTTAAAATCGCCCTCGAAATGCTATGTGAGCTGTGTGTGTGTGTGTGTGTGTGT
GTGTATTAAGGAAAAGCATGAAAGTATTTATGCTTGATTTTTTTTTTTTNACTCATAG
CTTCATAGTGGANCAGATACATAGTCTAAATCAAATGTTTAAACTTTTTATGTCAC
TTGCTGTC

FIG. 6



Telomeric element (E Tel) containing the survival motor-neuron gene (SMN gene). Genetic map shows polymorphic markers C212, C272 and C171. Physical map shows location and direction of transcription of SMN gene; phage clones used for assembling physical map. Restriction map for EcoRI(E), XbaI(X), HindIII(H), BglII(B), SacII(S) are shown. Cent. and Tel. indicate centromere and telomere respectively. The position of genomic rearrangements found in SMA patients are also indicated.



REPLACEMENT SHEET

GENE DOSAGE ANALYSIS OF THE 5q13 REGION WITH THE 132SE11 PLASMID CONE IN SMA TYPE I PATIENT. TOTAL HUMAN DNA FROM SMA FAMILY WAS DIGESTED WITH HindIII FOR SOUTHERN BLOTTING. FILTER WAS CONSECUTIVELY HYBRIDIZED WITH 132SE11 (A) AND JK53 PROBES (B). A SIGNIFICANT DECREASE IN 132SE11 BAND INTENSITY, WHICH INDICATED THE DELETION, COMPARED WITH THEIR PARENTS. F/FATHER, M/MOTHER, A/AFFECTED

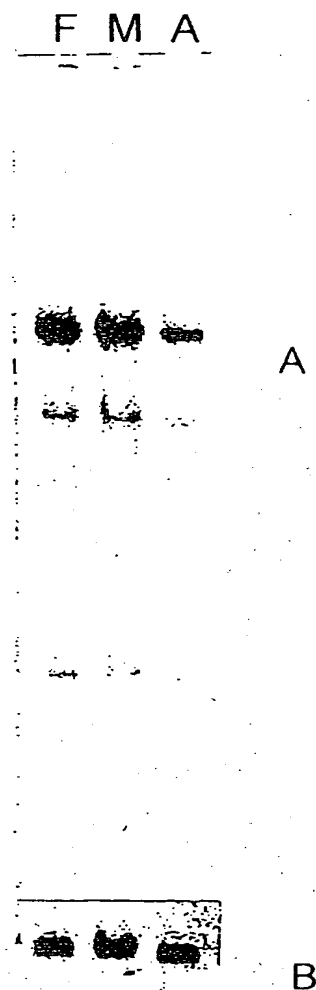


FIG. 7



REPLACEMENT SHEET

Figure 8

MAMSSGGSGGGVPEQEDSVLFRRGTGQSDDSDIWDDTALIKAYDKAVASFKHALKNG
DICETSGKPKTTPKRKPAKKNKSQKKNTAASLQQWKVGDKCSAIWSEDGCIYPATIA
SIDFKRETCVVVYTGYGNREEQNLSDLLSPICEVANNIEQNAQENENESQVSTDESE
NSRSPGNKSDNIKPKSAPWNSFLPPPPMPGPRLGPGKPGGLKFNGPPPPPPPPPHL
LSCWLPPFPSGPPIIPPPPPICPDSLDDADALGSMLISWYMSGYHTGYM





REPLACEMENT SHEET

Figure 10A

1

cctccccgggcaccgtactgttccgctcccagaagccccgggcccgggaagtgcgtcac
tcttaagaagggacgggggccccacgctgcgcaccccgcggtttgct ATG GCG

M A

ATG AGC AGC GGC GGC AGT GGT GGC GGC GTC CCG GAG CAG GAG
M S S G G S G G G V P E Q E
GAT TCC GTG CTG TTC CGG CGC GGC ACA GGC CAG gtgagggtcgcagc
D S V L F R R G T G Q

cagtgcagtctccctatttagcgctctcagcacccttcttcggcccaactctccttc
cgca

2a

gtgtaattttgttatgtgtggattaagatgactccttggtactaacatacattttctg
attaaacctatctgnacatgagttgtttttattttcttaccctttccag AGC GAT

S D

GAT TCT GAC ATT TGG GAT GAT ACA GCA CTG ATA AAA GCA TAT
D S D I W D D T A L I K A Y
GAT AAA GCT GTG GCT TCA TTT AAG gtatgaaatgcttgnttagtcgttt
D K A V A S F K

tcttattttctcgttatttcatttggaaggaattgataacatacgataaagtgttaa

2b

agggtgctttctgaggtgacggagccttgagactagcttatagtagtaactgggttat
gtcgtgactttttatttctgtgcaccaccctgtaacatgtacattttttatttctatttt
cgtag CAT GCT CTA AAG AAT GGT GAC ATT TGT GAA ACT TCG GGT

H A L K N G D I C E T S G

AAA CCA AAA ACC ACA CCT AAA AGA AAA CCT GCT AAG AAG AAT
K P K T T P K R K P A K K N
AAA AGC CAA AAG AAG AAT ACT GCA GCT TCC TTA CAA CAG gttat
K S Q K K N T A A S L Q Q

tttaaaatgttgaggatttaacttcaaaggatgtctcattagtccttattttaatagt
gtaaaatgtctttaact

3

gcctgcagggtcgatcaaaacgagatgatagtttgccctcttcaaaagaaatgtgtgc
atgtatatatctttgatttctttttag TGG AAA GTT GGG GAC AAA TGT

W K V G D K C

TCT GCC ATT TGG TCA GAA GAC GGT TGC ATT TAC CCA GCT ACC
S A I W S E D G C I Y P A T
ATT GCT TCA ATT GAT TTT AAG AGA GAA ACC TGT GTT GTG GTT
I A S I D F K R E T C V V V
TAC ACT GGA TAT GGA AAT AGA GAG GAG CAA AAT CTG TCC GAT
Y T G Y G N R E E Q N L S D
CTA CTT TCC CCA ATC TGT GAA GTA GCT AAT AAT ATA GAA CAG
L L S P I C E V A N N I E Q



REPLACEMENT SHEET

Figure 10B

AAT GCT CAA GAG gtaaggatacaaaaaaaaaaattcaatttctggaagcag
N A Q E
agactagatgagaaactgttaaacagtatacaca

4

ccaccgaggcattaatttttttcttaatcacacccttataacaaaaacctgcatattt
tttcttttttaaag AAT GAA AAT GAA AGC CAA GTT TCA ACA GAT GAA
N E N E S Q V S T D E
AGT GAG AAC TCC AGG TCT CCT GGA AAT AAA TCA GAT AAC ATC
S E N S R S P G N K S D N I
AAG CCC AAA TCT GCT CCA TGG AAC TCT TTT CTC CCT CCA CCA
K P K S A P W N S F L P P P
CCC CCC ATG CCA GGG CCA AGA CTG GGA CCA GGA AAG gtaaactt
P P M P G P R L G P G K
ctatgaaagttttccagaaaatagttaatgtcgggacatttaacctctctgttaact
aattttagctctccca

5

caaataattctgggtaattatttttatccttttggttttgagtcctttttatttcctat
catattgaaattggtaagttaattttcctttgaaatattccttatag CCA GGT
P G
CTA AAA TTC AAT GGC CCA CCA CCG CCA CCG CCA CCA CCA CCA
L K F N G P P P P P P P P P
CCC CAC TTA CTA TCA TGC TGG CTG CCT CCA TTT CCT TCT GGA
P H L L S C W L P P F P S G
CCA CCA gtaagtaaaaaagagtataggttagattttgctttcacatacaatttga
P P
taatta

6

ccagactttacttttttggtttactggatataaacaatatctttttctgtctccag
ATA ATT CCC CCA CCA CCT CCC ATA TGT CCA GAT TCT CTT GAT
I I P P P P P I C P D S L D
GAT GCT GAT GCT TTG GGA AGT ATG TTA ATT TCA TGG TAC ATG
D A D A L G S M L I S W Y M
AGT GGC TAT CAT ACT GGC TAT TAT ATG gtaagtaatcactcagcatct
S G Y H T G Y Y M
tttcttgacaatttttttgtagttatgtgactttggttggttaaatttataaaatact
acttg

7

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atcaacttaatttctgatcatattttggttgaaataaaataagtaaaatgtcttgtaa



REPLACEMENT SHEET

Figure 10C

→ a
acaaaatgctttttaacatccatataaagctatctatatatagctatctatgtctat

→ T
atagctatttttttaacttccttttattttccttacag GGT TTC AGA CAA
G F R Q
AAT CAA AAA GAA GGA AGG TGC TCA CAT TCC TTA AAT taaggagta
N Q K E G R C S H S L N *
aagtctgccagcattatgaaagtgaatcttacttttgtaaaactttatgggtttgtgg

→ g
aaaacaaatgtttttgaacagttaaaaagttcagatgttaaaaagttgaaagggttaa
tgtaaaacaatcaatattaaagaattttgatgccaaaactattagataaaaagggttaa

→ g
tctacatccctactagaattctcacttaactgggttggttatgtggaagaaacata
ctttcacaataaagagcttttaggatatgatgccattttatatcactagtaggcagac
cagcagacttttttttattgtgatatgggataacctaggcactactgcactgtacact
ctgacatatgaagtgtcttagtcaagtttaactgggtgtccacagaggacatgggtta

8
actggaattcgtcaagcctctgggttctaattttctcatttgcaggaaatgctggcata
gagcagcactaaatgacaccactaaagaaacgatcagacagatctggaatgtgaagc
gttatagaagataactggcctcattttcttcaaaatatcaagtgttgggaaagaaaaa
aggaagtggaatgggtaactcttcttgattaaaagttatgtaataaccaaataatgcaat

→ a
gtgaaatattttactggactcttttgaaaaaccatctagtaaaagactgggggtgggg
gtggggaggccagcacggtggtgaggcagttgagaaaatttgaaatgtggattagattt
tgaatgatattggataattattggtaattttatggcctgtgagaaggggtgtttagt
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REPLACEMENT SHEET

Figure 11

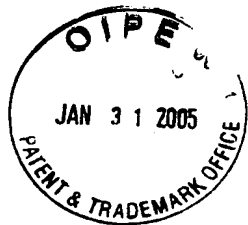
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tatagatcaagcagggttttaaattcctagtaggagcttacattttactttt 100
ccaaggggggagggggaataaatatctacacacacacacacacacacca 150
 H4TF-1 GH
cactggaggttcgagacgaggcctaagcaacatgccgaaaccccgctctta 200
 DTF-1
ctaaatacaaaaaaatagctgagcttggtggcgacgcctatagtcctagc 250
tactggggaggctgaggtgggaggatcgcttgagcccaagaagtcgaggc 300
 Sp1
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aggctctgtctcaaaacaaacaaacaaaaaaaaaaaaaggaaaggaaatata 400
 β-IFN
acacagtgaatatgaaaggattgagagaaatgaaaaatatacacgccacaa 450
 HiNF-A
atgtgggagggcgataaccactcgtagaaagcgtgagaagttactacaag 500
cggtcctcccgggcaccgtactgttccgctcccagaagccccggggcgccg 550
 AP-2
gaagtcgtcactcttaagaaggacggggccccacgctgcgcacccgcgg 600
 E4F1
gtttgct ATG GCG ATG AGC AGC GGC GGC AGT GGT GGC 637
 M A M S S G G S G G



REPLACEMENT SHEET

Figure 12B

AGC	AAG	TCC	AAA	GCT	GCT	CCG	TGG	ACC	TCA	TTT	CTT	CCT	587
Ser	Lys	Ser	Lys	Ala	Ala	Pro	Trp	Thr	Ser	Phe	Leu	Pro	
CCA	CCA	CCC	CCA	ATG	CCA	GGG	TCA	GGA	TTA	GGA	CCA	GGA	626
Pro	Pro	Pro	Pro	Met	Pro	Gly	Ser	Gly	Leu	Gly	Pro	Gly	
AAG	CCA	GGT	CTA	AAA	TTC	AAC	GGC	CCG	CCG	CCG	CCG	CCT	665
Lys	Pro	Gly	Leu	Lys	Phe	Asn	Gly	Pro	Pro	Pro	Pro	Pro	
CCA	CTA	CCC	CCT	CCC	CCC	TTC	CTG	CCG	TGC	TGG	ATG	CCC	704
Pro	Leu	Pro	Pro	Pro	Pro	Phe	Leu	Pro	Cys	Trp	Met	Pro	
CCG	TTC	CCT	TCA	GGA	CCA	CCA	ATA	ATC	CCG	CCA	CCC	CCT	743
Pro	Phe	Pro	Ser	Gly	Pro	Pro	Ile	Ile	Pro	Pro	Pro	Pro	
CCC	ATC	TCT	CCC	GAC	TGT	CTG	GAT	GAC	ACT	GAT	GCC	CTG	782
Pro	Ile	Ser	Pro	Asp	Cys	Leu	Asp	Asp	Thr	Asp	Ala	Leu	
GGC	AGT	ATG	CTA	ATC	TCT	TGG	TAC	ATG	AGT	GGC	TAC	CAC	821
Gly	Ser	Met	Leu	Ile	Ser	Trp	Tyr	Met	Ser	Gly	Tyr	His	
ACT	GGC	TAC	TAT	ATG	GGT	TTC	AGA	CAA	AAT	AAA	AAA	GAA	860
Thr	Gly	Tyr	Tyr	Met	Gly	Phe	Arg	Gln	Asn	Lys	Lys	Glu	
GGA	AAG	TGC	TCA	CAT	ACA	AAT	taag						885
Gly	Lys	Cys	Ser	His	Thr	Asn	*						



REPLACEMENT SHEET

Figure 13

20 30 40 50 60 70
GSGGGVPEQEDSVLFRRGTGQSDDSDIWDDTALIKAYDKAVASFKHALKNGDICETS
=====
GSGGAGSEQEDTVLFRRGTGQSDDSDIWDDTALIKAYDKAVASFKHALKNGDICETP
20 30 40 50 60

80 90 100 110 120 130
GKPKTTPKRKPAKKNKSQKKNNTAASLQWKVGDKCSAIWSEDGCIYPATIASIDFKR
=====
DKPKGTTARRKPAKKNKSQKKNATTPLKQWKVGDKCSAVWSEDGCIYPATITSIDFKR
70 90 100 110 120

140 150 160 170 180 1
ETCVVVYTGYGNREEQNLSDLLSPICEVANNIEQNAQENENESQVSTDESENSRSPG
=====
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130 140 160 170 1

90 200 210 220 230 240
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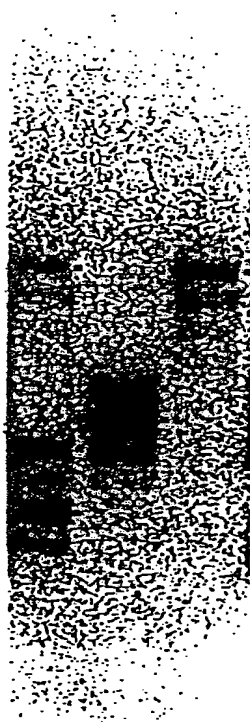
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SL

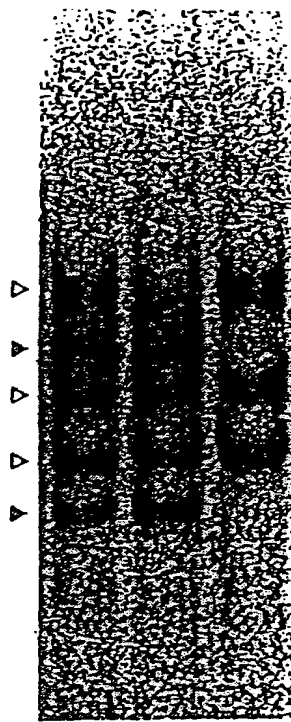
TN



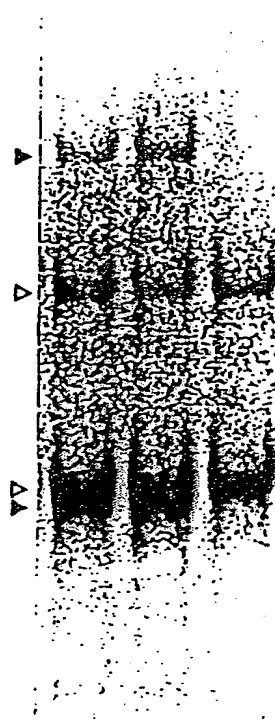
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F M A



F M A



F M A

FIG. 14(A) FIG. 14(B) FIG. 14(C)



SSCP ANALYSIS

▼ SMN
▽ C-BCD541



121B8 YAC
595CII YAC
HUMAN 1 CONTROL
HUMAN 2 CONTROL
HUMAN 3 CONTROL
HUMAN 4 SMA

FIG. 15

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